of a potentially lethal tissue hypersensitivity. Attempts to show that the Behring "paradox" was a "summative phenomenon" due to cumulative tissue injury from previous toxin injections were unsuccessful. In some of the reported experiments the sum of all previous doses of tetanus toxin was less than a single MLD for a normal guinea pig.

In spite of the fact that many investigators failed to confirm the Behring paradox, the Ehrlich interpretation of this phenomenon became a generally accepted dogma in practical immunology. It was apparently self-evident that immunization of patients by multiple injections with bacterial toxins was clinically dangerous.

In order to attack this clinical dogma, the German investigators repeated the original Behring experiments with a sufficiently large number of animals and toxins to be statistically conclusive. Groups of guinea pigs of equal weight, size, and age were injected subcutaneously with multiple doses of diphtheria tetanus, dysentery toxin, or snake venom, the size of the dose being doubled with each subsequent injection, until a lethal reaction was produced.

Out of all of his series, only three guinea pigs gave quasi-Behring reactions. One guinea pig, for example, died twenty-four hours after the first injection of about 1/1000 MLD dysentery toxin. In all three of these atypical cases necropsy showed atypical histologic changes, from which it was concluded that the deaths could not be solely attributed to the toxin injected. All other animals of the series exhibited no toxic symptoms till the daily dose was increased to at least one MLD. Two MLD was the approximate average lethal dose for these partially immunized animals. An appreciable immunity, therefore, was developed in each series, with no suggestion of an acquired toxin hypersusceptibility.

Of even greater clinical interest is the series injected with nontoxic diphtheria toxoid. After the eighteenth injection—that is, at the height of the predictable Ehrlich hypersensitivity—the entire series was divided into subgroups, and tested with unit and subunit doses of active diphtheria toxin. None of the animals tested with less than one MLD died of the active toxin. There was, therefore, no demonstrable toxin hypersusceptibility. All animals injected with one MLD survived the test, showing an appreciable immunity. In most cases at least two MLD were necessary to cause death.

Hiroki's general conclusion from his data is that a toxin hypersensitivity is not a necessary concomitant of an acquired antitoxic immunity. He believes that Behring's much published "paradox" was due to experimental or statistical errors, presumably to a few unsuspected subnormal or virus-infected animals which died of other causes during the course of his immunization, or to mistakes of his technicians in making toxin dilutions. Hiroki concludes from his data that an acquired humoral immunity is invariably accompanied by an underlying acquired tissue immunity, and not by the "mythological" tissue hypersusceptibility deduced from the Ehrlich theory. Errors in the Ehrlich theory, of course, have long been recognized by American immunologists.[3]

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RECENT DEVELOPMENTS IN THE BACTERIOLOGY AND TREATMENT OF URINARY INFECTIONS

Interest in the bacteriology and treatment of urinary infections has increased greatly in the past few years. Knowledge of the effects upon urinary infections of the reaction of urine, of metabolic products as beta-hydroxybutyric acid, and chemicals, as mandelic acid and sulfanilamide, have opened new fields for treatment. The fact that various bacteria are affected to different degrees by the same therapeutic agent, and that new chemicals are constantly being introduced, make it important to keep abreast of new findings.

The pathogenicity of various urinary infectants was investigated by Goldstein in 1938. He injected cultures of Streptococcus fecalis, Staphylococcus aureus, and Micrococcus into rabbits. Streptococcus fecalis produced lesions in 37 per cent of nineteen rabbits, pathologically mostly pyelitis, and a larger dose was required than in the case of Staphylococcus aureus, which caused renal lesions in 73 per cent of eleven rabbits. Micrococcus produced no lesions in the fourteen animals into which it was injected, and the urine remained normal in contrast to that of the animals injected with the other organisms.

Recently, Schulte introduced several new methods of studying the bacteriology of the urinary tract. He reported (1) the use of a new medium containing urea for the determination of urea-splitting organisms; (2) and a presumptive test for coagulase, which differentiates virulent mass-forming Gram-positive cocci from nonvirulent; the virulent Staphylococci were shown to coagulate human or horse plasma, while Micrococci did not exhibit this property; and (3) he determined the specific virulence of organisms by animal injections, including urea-splitters as Staphylococcus and Proteus.

The history of chemotherapy of urinary infections has shown rapid strides since Shohl and Janney in 1917 proved the value of acidification in destroying the commoner bacilli infecting the urinary tract. The use of mandelic acid for urinary infections, following the reports of Rosenheim in 1935, almost revolutionized the chemotherapeutic armamentarium of the urologist. Results obtained with this drug far exceeded those previously reported. However, where a low p^H could not be secured, or when there was not an adequate renal function to produce the needed concentration of mandelic acid or degree of acidity, the drug would not act bactericidally.

[3] Jordan, E. O., and Falk, I. S.: "Newer Knowledge of Bacteriology and Immunology," Chap. 81, p. 1078, University of Chicago Press, 1928.

The need, therefore, was for a drug which would act in an alkaline urine and not require the renal function necessary with the previously used drugs. At this point, in 1937, sulfanilamide began coming into use, in this country, for Streptococcal infections. Helmholz investigated its use as a urinary antiseptic and found that it created a bactericidal urine which acted against most of the common urinary invaders.

Following this experiment, it was found by Buchtel and Cook that sulfanilamide was more bactericidal for bacillary than for coccal infections, especially the Streptococcus fecalis. They also showed that the drug was excreted by the prostate, but in lower concentration than in the urine.

More recently, Cook used neoprontosil soluble orally in urinary infections, and found fewer reactions than with sulfanilamide. As with mandelic acid and sulfanilamide, neoprontosil soluble was found of most value in uncomplicated cases caused by the usual Gram-negative bacilli, the beta hemolytic Streptococci, or some of the Micrococci.

At present sulfapyridine is another drug which is being tested widely for its efficacy in urinary tract infections, and its value should be known shortly. Other drugs will undoubtedly be offered the medical profession in the near future, but none should be accepted until careful investigation has proved its worth.

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DIFFERENTIAL COUNT FOR SPERMATOZOA

There has been a great deal of interest shown lately in the differential count of spermatozoa. The following method of staining is quite satisfactory and not at all complicated:

The semen should be diluted with ten parts of Ringer's solution with 0.5 per cent chloramin added, and centrifuged strongly for twenty minutes or more; the supernatant liquid poured off, and the sediment spread on a slide as for a blood smear. (The fresh specimen should be examined microscopically before making the smear, and the smear should be made thick or thin, according to the density of the sperm population.)[1]

The smear is then dried, fixed in methyl alcohol and washed with distilled water.

Stain with Sterling's gentian violet, one per cent, one-half to one minute. (Williams uses gentian violet, one-fourth of one per cent, for four or five minutes.)[2]

Wash in distilled water.

Place in Gram's iodin one minute.

Decolorize in alcohol, 80 per cent, acetone, 20 per cent, not over one-half minute.

Counterstain ten to thirty seconds with rose bengal.

Wash in distilled water.

Dry and examine with the 1/12 (oil).

If a permanent smear is desired, mount with balsam and cover slip.

This stain is a modification of that given by W. W. Williams.[3]

Hotchkiss'[4] method of staining, though more complicated, is better for permanent smears.

Moench's[5] stain is very satisfactory, but chloramin is better than chlorozene for removing mucus.

A fresh wet specimen should be studied, both with the H. D. F. and oil, and compared with the findings of the stained smear for proper evaluation.

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USES AND ABUSES OF PITUITARY EXTRACT DURING LABOR

There is no question that posterior pituitary preparations have been woefully misused in the conduct of obstetric cases. They have been given indiscriminately in the first and second stages of labor to increase the intensity of uterine action, and to speed up the normal processes. DeLee, and others, feel that the injudicious and indiscriminate use of the pituitary preparations is one of the major factors contributing to the persistently high maternal and fetal death rates in the United States.

Any oxytocic given, with or without proper indications, can kill both mother and baby. These oxytocic drugs are really never indicated in the first or second stages of labor. It is dangerous to interfere with the normal uterine motility.

Posterior pituitary extract used during labor initiates marked tetany of the uterus; as this tone diminishes, the uterine contractions increase in severity and frequency. This abnormal uterine action may result in interference with the placental circulation, resulting in fetal asphyxia, and even death. It may, likewise, result in interference with the uterine circulation and, subsequently, damage the uterine musculature.

Other uterine conditions which may result from injudicious use of pituitary extract are rupture of the uterus; laceration of the cervix with hemorrhage or infection; secondary atony of the uterus with thrombosis and embolism, and even cardiac death from sudden overexertion.

It is true that many doctors use small doses of pituitary extract during the second stage of labor and claim no untoward results. However, one never knows how an individual may react, and rather than take a chance with life the drug should be used only when indicated, and that is in the third stage of labor. Used judiciously and with the proper indications, the oxytocic drugs often prevent the occurrence of postpartum hemorrhage and the serious results that may be caused by it.

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1 Lane Roberts et al.: Sterility and Impaired Fertility, Paul Hoeber, Inc., N. Y., 1939.
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3 Suggested by H. P. Oliver, M. D.
4 Hotchkiss, R. S.: Semen Appraisal, J. A. M. A., 102: 587-590, (Feb. 24), 1934.
5 Moench, G. L.: Clinical Laboratory Methods and Diagnosis, Gradwohl, 2nd ed., p. 710, 1938.